

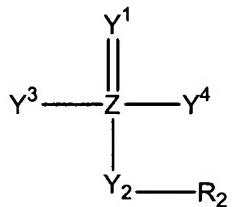
Applicant : Thomas J. McMurry, et al.  
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REMARKS

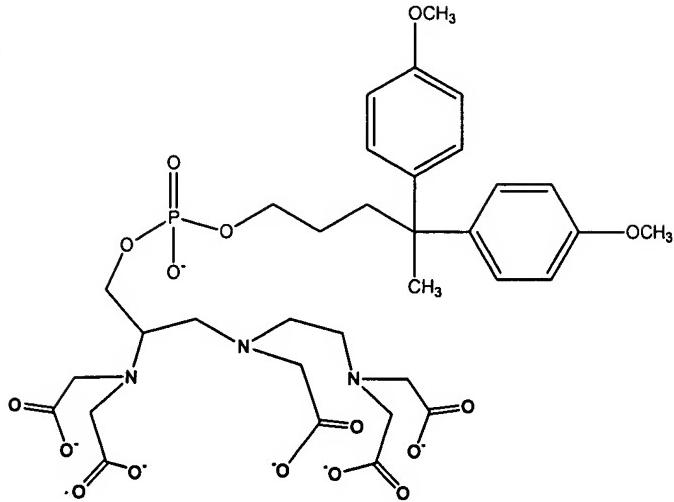
Claims 1-18 were pending. Applicants have herein cancelled claims 1-18 and added new claims 103-117. Support for the claims may be found throughout the specification, e.g., at pages 8-11, 38, 40-42, 47-55, and 56-59. No new matter has been added. Applicants have also amended the priority information to cite the issued patent number in the parent case of the present application and to make reference to related cases. Accordingly, claims 103-117 are pending.

Applicants note that two different structures in the specification (e.g., compare structures at page 29 and page 30 of the specification) contained "R<sub>2</sub>" moieties. For clarity, Applicants have amended the specification to replace "R<sub>2</sub>" with -- R<sub>2</sub> -- in the following structure:

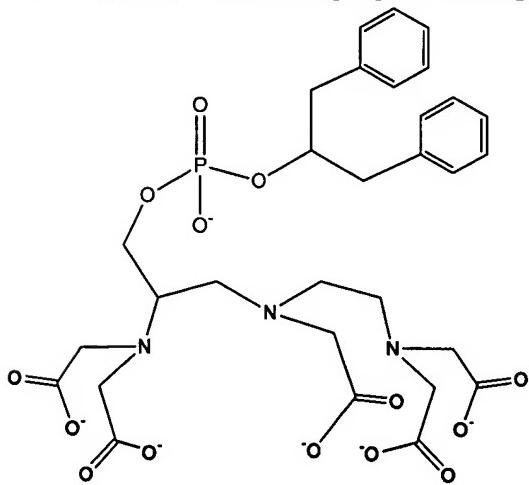


Applicants ask that all claims be examined in view of the amendment to the claims. The Examiner is invited to telephone the undersigned if such would expedite prosecution.

Enclosed is a \$842.00 check for excess claim and multiple dependent claim fees. Please apply any other charges or credits to deposit account 06-1050.



114. (New) A chelating ligand having the structure:



115. (New) A chelating ligand having the structure:

## COMMUNICATION

During a review of the present specification with various employees of the Assignee, it came to our attention that Examples 7-13 were arguably written in the incorrect tense when the application was filed. Examples 7-13 set forth methods for chelating a Gd(III) ion to the various chelating ligands described in the specification (e.g., MS-325; see page 38 of the specification). After interviewing the named inventors and various technical personnel at the Assignee, we determined that a named inventor, Dr. Thomas J. McMurry, had changed the examples from an earlier draft version. The method set forth in the earlier draft version had essentially added the base (e.g., N-methyl-glucamine, or NMG) to the  $\text{Gd}_2\text{O}_3$  and chelating ligand in two steps, rather than in a single step, as in the present specification Examples. Dr. McMurry indicated that he had shortened the chelation examples to a one-step addition of the base because he thought the earlier version included extraneous detail that was both unnecessary and lengthy. He pointed out that he had simply added the amounts of base (e.g., NMG) used in the earlier version and put that total amount down in a one-step reaction with the original amounts of  $\text{Gd}_2\text{O}_3$  and chelating ligand. Dr. McMurry also indicated that Gd(III) chelation was (and is) considered routine and standard chemistry, and that he thought that a one-step reaction (as written in the present specification) would work for all of the chelating ligands described in the specification.

The under-signed and her supervisor, Dr. Mark Ellinger, do not perceive any deceptive intent on the part of Dr. McMurry, or any of the named inventors, to misrepresent the correct method for chelation. We believe Dr. McMurry's statements that he had condensed the Examples to remove what he believed to be extraneous detail. In our opinion, Dr. McMurry had not appreciated that, in so doing, he had converted the Examples from actual to arguably prophetic in substance, with a technical requirement for a change in tense.

To confirm Dr. McMurry's beliefs that the one-step method in the specification would work as written, the Assignee repeated Example 10, setting forth the method for chelating the ligand of MS-325 with Gd(III). We had requested that the experiment be repeated exactly as written to determine if the example was an operable embodiment. It should be noted that Example 10 demonstrates the most substantive differences between the method set forth in the

earlier draft Examples section and the present specification. The experiment resulted in an 82% yield of the MS-325 Gd(III) chelate. A review of the Assignee's notebooks indicated that the two-step method set forth therein had a yield ranging from 76.5% to 99% for the various chelating ligands, including an 88% yield using the same ligand as in Example 10 in an experiment not included in the patent application.<sup>1</sup>

Based on our review of the relevant case law and the positive results of the Example 10 experiment, it is our opinion that the fact that the chelation examples were written in the past tense (i.e., as actual examples) versus in the present tense (i.e. as prophetic examples) is not material under 37 C.F.R. § 1.56.<sup>2</sup> We are, however, providing this information to the P.T.O. in an abundance of caution and in the interest of full disclosure. For the Examiner's convenience, we point out the holding in The Regents of the University of California v. Eli Lilly and Co., 119F.3d 1559 (Fed. Cir. 1997). In that case, the UC specification represented that a certain plasmid had been used in the examples, when a different plasmid actually had been used. The court noted that the defendant Lilly did not argue that the UC example was inoperable as written, but only that the examples "should not have been stated as actual examples (even though they presumably could have been stated as constructive, i.e., hypothetical examples.)" Id. at 1570. The court held that there was "no reason to believe that a reasonable examiner would have made any different decision if UC had framed [the examples] as constructive examples" and went on to hold that the misidentification of the plasmid was therefore not material to patentability. Id.<sup>3</sup> We also note that the court in Hoffmann-LaRoche, Inc., v. Promega Corp., 323 F.3d 1354, 1368 (Fed. Cir. 2003) distinguished the holding in that case from the Lilly holding by noting that the misidentification of the plasmid in UC's application did not make the examples inoperative; "rather the procedures described in the examples 'worked to yield the intended results

<sup>1</sup> We note also that the protocol for the experiment that had a yield of 88% was different from the protocol in Example 10, although they used the same ligand. The protocol having a yield of 88% was closer in substance to the one-step protocol that was included in the present application.

<sup>2</sup> See 37 C.F.R. § 1.56 and M.P.E.P. § 2001, defining information as "material" if it is not cumulative to information already of record and (1) it establishes by itself or in combination with other information, a *prima facie* case of unpatentability of a claim; or (2) it refutes or is inconsistent with, a position the applicant takes in: (i) opposing an argument of unpatentability relied on by the Office; or (ii) asserting an argument of patentability.

<sup>3</sup> The court also noted that the mischaracterization of the examples as actual examples did not induce the examiner to act, or not act, in reliance thereon.

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irrespective of' whether the actual plasmid was used, making the 'misidentification of the plasmid . . . not material to patentability (quoting Lilly).'''

Here, as confirmed by the Assignee, Example 10 worked effectively as written. As a consequence, the fact that Examples 7-13 are written in the past tense when, technically, they would more accurately have been written in the present tense, in our view is not material to examination. Neither do we believe that there was any deceptive intent on the part of Dr. McMurry or any other named inventor with respect to this issue. The Examiner is invited to telephone the under-signed if such would assist the Examiner in his/her understanding of this matter.

Respectfully submitted,

Date: 1/15/04

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